The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board

Paper No. 20

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte TSUE-MING LIN and SEYMOUR P. HALBERT

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Appeal No. 1997-4138
Application No. 08/384,681

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HEARD: January 9, 2001

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Before WINTERS, ROBINSON, and GRIMES, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 27 - 44, 46 - 52, and 54 - 63 which are all of the claims pending in the case.

Claims 27, 46, and 56 are illustrative of the subject matter on appeal and read as follows:

27. A test kit for detecting the presence in a sample of at least one component to be detected selected from the group consisting of antigens, antibodies and haptens by a sandwich enzyme immunoassay comprising in one or more containers:

a. An analytical device consisting essentially of an inert, opaque plastic carrier having a flat, hydrophobic surface that is non-absorbent to said antigens, antibodies, haptens and to enzymes, having a multiplicity of visually locatable discrete locations and, deposited directly on said surface within at least one of said discrete locations, a spot of an insolubilized specific first binding partner of the at least one component to be detected;

b. a working reagent conjugate of predetermined concentration of at least about 15 micrograms per ml in liquid form comprising an enzyme coupled to a specific second binding partner of the at least one component to be detected; and

c. an enzyme substrate in liquid form comprising a material capable of reacting with said enzyme at room temperature to form a colored precipitate detectable by the naked eye against said opaque carrier.

46. A sandwich enzyme-immunoassay process for detecting the presence in a sample from the group consisting of body fluid and the body fluid diluted 1:10 or less of at least one component to be detected selected from the group consisting of antigens, antibodies and haptens, comprising:

a. applying a drop of said sample onto one of a plurality of visually locatable, discrete locations on a flat, hydrophobic surface, that is non-absorbent to said antigens, antibodies and haptens and to enzymes, of an inert, opaque plastic carrier, said location having deposited directly thereon a spot of insolubilized specific, first binding partner of the at least one component to be detected;

b. incubating said carrier for up to one-half hour to immobilize said at least one component to be detected;

c. removing unbound body fluid;

d. applying onto each of said discrete locations a drop of a second fluid comprising at least 15 micrograms per ml of a conjugate of an enzyme coupled to a specific second binding partner of the component to be detected;

e. incubating at room temperature for up to one-half hour to immobilize said conjugate;

f. washing away unbound conjugate;

g. applying onto said discrete location a drop of a second fluid comprising a substrate reactable with said enzyme at room temperature to form within about five minutes a colored precipitate visually detectable against said opaque carrier; and

h. visually ascertaining the presence or absence of the colored precipitate as indicative of the presence or absence of said at least one component to be detected.

56. An analytical device for use in a sandwich enzyme immunoassay for detecting the presence in a body fluid of at least one component to be detected selected from the group consisting of antigens, antibodies and haptens, consisting essentially of an inert, opaque plastic carrier having a flat, hydrophobic surface that is non-absorbent to said antibodies, antigens and haptens and to enzymes having deposited directly thereon an insolubilized specific binding partner of the at least one component to be detected in the form of spots of from 1 to 4 mm in diameter in discrete, visually locatable locations.

The references[1] relied upon by the examiner are:

Fish et al. (Fish) 5,126,276 Jun. 30, 1992

Towbin et al. (Towbin), "Immunoblotting and Dot Immunobinding -- Current Status and Outlook," Journal of Immunological Methods, vol. 72, pp. 313-340, 1984

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[1] At page 11 of the Examiner's Answer, the examiner cites U.S. Patent 4,594,225 to Arai et al. Since this reference was not included in the list of references relied upon and not included in the statement of the rejection, it is not clear whether the reference is relied upon to establish the state of the prior art. If it is relied upon to establish the state of the art relative to a rejection under 35 U.S.C. § 103, the record should clearly indicate that it is so relied upon and appellants given ample opportunity to respond thereto. In view of the confusion as to the status of the examiner's reliance on this reference, we have not considered it in considering the issues raised by this appeal. When a reference is relied on to support a rejection even in a "minor capacity," ordinarily that reference should be positively included in the statement of rejection. In re Hoch, 428 F.2d 1341, 1342, n.3, 166 USPQ 406, 407, n. 3 (CCPA 1970).

European Patent Applications:

Gordon et al. (Gordon)	0 063 810	Nov. 3, 1982
Wada	0 125 118	Nov. 14, 1984

GROUNDS OF REJECTION

Claims 27 - 31, 33 - 35, 41 - 42, 46 - 52, 54 - 55, and 62 -63 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Fish.

Claims 27 - 31, 41 - 42, 46 - 52, 54 - 55, and 62 -63 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Fish and Wada.

Claims 36 - 40, 43 - 44, and 56 - 61 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Fish, Gordon, and/or Towbin.

Claims 36 - 40, 43 - 44, and 56 - 61 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Fish, Wada, Gordon, and/or Towbin.

We reverse.

BACKGROUND

Applicants describe the invention at pages 4 and 7 of the specification, as being directed to a dot test for assaying body fluids for components, such as antigens, antibodies, and haptens, employing an enzyme-immunoassay technique and a kit of reagents for carrying out the assay. The kit is stated to include a white opaque plastic card, such as high impact hydrophobic polystyrene, having identifiable small spots or

dots thereon which contain an insolubilized binding partner of the component to be determined.

DISCUSSION

The rejections under 35 U.S.C. § 103

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicants. Id. In order to meet that burden the examiner must provide a reason, based on the prior art, or knowledge generally available in the art as to why it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297 n.24, 227 USPQ 657, 667 n.24 (Fed. Cir. 1985), cert. denied, 475 U.S. 1017 (1986).

Claims 27 - 31, 33 - 44, 46 - 52, 54-55, and 62 - 63:

On the record before us, the examiner has not met the initial burden of establishing why the prior art relied on would have led one of ordinary skill in this art to modify the assay of Fish, Wada, Gordon, or Towbin in a manner to arrive at the presently claimed assay kit (Claim 27) or assay (Claim 46), both of which require the presence or use of "a working reagent conjugate of predetermined concentration of at least about 15 micrograms per ml

in liquid form comprising an enzyme coupled to a specific second binding partner of the at least one component to be detected." The examiner acknowledges that (Answer, page 6):

> Fish differs [from the claimed invention] in failing to disclose the concentration of the probe (either stock or working solution).

The examiner does not allege that the remaining references provide that which is missing from Fish. Instead the examiner concludes that (Answer, pages 6-7):

> [i]t would have been a matter of routine optimization well within ordinary skill in the art to ascertain an acceptable concentration of probe or sample dilution, such as that specifically claimed, because the particular concentration of probe required depends upon the antibody used and the enzyme used, e.g.[,] how avid the antibody is to begin with; how active the enzyme preparation is; how much inactivation of the antibody and/or enzyme occurs as a result of the conjugation process; the molar ratio of antibody/enzyme in the probe, etc. These factors can vary widely for different conjugate, particularly when monoclonal antibodies are used. Thus, use of a particular concentration of conjugate carries little patentable weight, especially where the recited concentration may refer to either a stock solution which can be further diluted to form a working solution or to the working solution itself.

What is missing from this analysis and the conclusion reached is any evidence which would establish that this information was within the knowledge of one of ordinary skill in this art at the time of the invention and which would reasonably support either

the importance of these factors in determining the concentration of the probe solution to be used in this type of assay or some indication of how such factors would direct one of ordinary skill in this art to vary the concentration of the probe solution. Thus, the examiner's statements in support of the rejection of claims 27 - 31, 33 - 44, 46 - 52, 54, 55, 62, and 63 directed to the assay kit and the assay are not supported by those facts or evidence which would have suggested or directed one or ordinary skill in this art to modify the teaching of Fish alone, or when taken in combination with Gordon, Wada or Towbin, in the manner required to arrive at the claimed invention. To the extent that the examiner relies on Towbin as suggesting the use of a concentrated solution, we note that the examiner acknowledges that (Supplemental Answer, page 4) "Appellant is correct in noting Towbin is referring to providing a more concentrated immobilized antigen, to provide a more concentrated reaction which would have been expected to generate a better contrast of the color generated by the reaction against the background." Further, this teaching does not suggest or direct one or ordinary skill in the art to use a more concentrated solution, and particularly a specific concentration, of the probe solution in such an assay.

On these facts, we are constrained to find that the examiner has failed to establish that it would have been obvious to those of ordinary skill in the art at the time of the invention to provide a kit or assay which requires having a working reagent

conjugate of predetermined concentration of at least about 15 micrograms per ml in liquid form as claimed. The only source of a suggestion to use the particular concentration of the working reagent presently claimed is appellants' own disclosure of the invention. Therefore, we must conclude that the examiner has relied on impermissible hindsight in making his determination of obviousness. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps").

For these reasons, the examiner's rejections of the claims, directed to the assay and kit for performing the assay, are fatally defective since they do not properly account for and establish the obviousness of the claimed subject matter as a whole. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Therefore the rejections of claims 27 - 31, 33 - 44, 46 - 52, 54-55, and 62 - 63 under 35 U.S.C. § 103 are reversed.

Claims 56 - 61:

Claims 56 - 61 stand on a different footing as compared to the claims directed to an immunobinding assay and a kit for performing such an assay discussed above. Claims 56 - 61 do not require the presence or use of a working reagent conjugate of

predetermined concentration of at least about 15 micrograms per ml in liquid form.

The examiner has rejected claims 56 - 61 over Fish in combination with Gordon or Towbin and if necessary in view of Wada. (Answer, page 3). The examiner relies on Gordon as disclosing "direct application of antigens, immunoglobulins or both to microporous solid supports in any suitable preselected geometry, e.g., in the form of dots (page 11, line 5) or in a 3x3 mm grid pre-printed on the support (page 18, line 11)." (Answer, page 7). The examiner relies on Towbin as describing "direct dot/spot application of the dots to a defined location and the subsequent cutting of strips of desired geometry." (Id.) The examiner concludes (Answer, paragraph bridging pages 7-8):

> It would have been obvious to one of ordinary skill in the art to modify the methods, devices and kits of Fish by utilizing direct application of receptors in any suitable preselected geometry, such as within a "grid" work as suggested by either Gordon or Towbin for the same intended purpose of easy application to define locations, etc.

However, claim 56 requires more than just a grid work to provide a preselected geometry for placement of the reagents. Claim 56 requires that the device consist essentially of an inert, opaque plastic carrier having a flat hydrophobic surface that is non-absorbent to said antibodies, antigens, haptens, and enzymes. In addition, the plastic carrier has deposited directly thereon an insolubilized specific binding partner in the form of spots of from 1 to 4 mm in diameter in discrete, visually locatable locations. Thus, in order to arrive at the claimed invention, Fish would have to be modified by depositing the

insolubilized specific binding partner of the component to be detected in the form of spots of a particular diameter in discrete, visually locatable locations. Gordon and Towbin would teach those skilled in this art at the time of the invention to use a spot or drop technique to apply the first specific binding partner to the solid support. However, both of these references would reasonably appear to suggest that the solid support must be a porous material which allows the binding partner to adhere in a certain quantity to the surface of the solid support. (Gordon, page 3, second paragraph and page 4, last paragraph; Towbin, page 336, Concluding Remarks). Thus, in order to modify Fish to use the spot or drop application and grid locator of Gordon and/or Towbin, one would also be directed to modify the solid support of Fish to provide a porous base on which to apply the binding partner. In fact, Gordon contemplates the use of solid supports such as those described in Fish and the claimed device in the assay described. However, Gordon also specifies that the solid support, e.g., polystyrene, must be suitably porous structures. (Gordon, page 9, paragraph D). Thus, if we modify Fish using the direction provided by Gordon and Towbin, the resulting assay device would no longer be expected to have a flat, hydrophobic, non-absorbent surface as required by claim 56. Wada does not provide that which is missing from the combined teachings discussed. As stated in In re Hedges, 783 F.2d

1038, 1039, 228 USPQ 685, 686 (Fed. Cir. 1986); quoting from In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965): "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art."

Thus, on this record, if the references were combined in the manner urged by the examiner, one would not arrive at the claimed device. The examiner has failed to provide those facts and evidence which would reasonably establish a prima facie case of obviousness within the meaning of 35 U.S.C. § 103 as to claims 56 - 61. Therefore, we reverse the rejection of claims 56 - 61 under 35 U.S.C. § 103 as obvious over the combination of Fish, Gordon, Wada, and Towbin.

CONCLUSION

The examiner's rejections of claims 27 - 44, 46 - 52, and 54 - 63 under 35 U.S.C. § 103 as obvious over Fish alone or over the combined teachings of Fish, Gordon, Wada and Towbin are reversed. Having determined that the examiner failed to establish a prima facie case of obviousness as to the claimed subject matter, we have not found it necessary to considered the declaration evidence provided by appellants.

REVERSED

SHERMAN D. WINTERS Administrative Patent Judge	)	
DOUGLAS W. ROBINSON Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
ERIC GRIMES Administrative Patent Judge	)	

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